```
=> s inhibit?(l)((serine or threonine)(l)kinas?)
       2048104 INHIBIT?
        120825 SERINE
         64073 THREONINE
        333798 KINAS?
L1        8443 INHIBIT?(L)((SERINE OR THREONINE)(L)KINAS?)

=> s l1 and (indaz?(5w)pyrid?) or (triaz?(5w)pyrid?) or (pyrrol?(5w)pyrid?))
UNMATCHED RIGHT PARENTHESIS 'PYRID?))'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l1 and ((indaz?(5w)pyrid?) or (triaz?(5w)pyrid?) or (pyrrol?(5w)pyrid?))
          6210 INDAZ?
        395477 PYRID?
           171 INDAZ?(5W)PYRID?
        113272 TRIAZ?
        395477 PYRID?
          3144 TRIAZ?(5W)PYRID?
        159235 PYRROL?
        395477 PYRID?
          5272 PYRROL?(5W)PYRID?
L2          27 L1 AND ((INDAZ?(5W)PYRID?) OR (TRIAZ?(5W)PYRID?) OR (PYRROL?(5W)
               PYRID?))

=> d bib abs 1-27

L2   ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2008:160612  CAPLUS
DN   148:215061
TI   Preparation of 2-heterocyclyl-1,3,4-oxadiazole derivatives as glycogen
     synthase kinase-3β (GSK-3β) inhibitors
IN   Itoh, Fumio; Kunitomo, Jun; Kobayashi, Hiromi; Kimura, Eiji; Saitoh,
     Morihisa; Kawamoto, Tomohiro; Iwashita, Hiroki; Murase, Katsuhito
PA   Takeda Pharmaceutical Company Limited, Japan
SO   PCT Int. Appl., 531pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
PI   WO 2008016123        A1    20080207    WO 2007-JP65203        20070802
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
             MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
             PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
PRAI JP 2006-212642       A     20060803
OS   MARPAT 148:215061
GI
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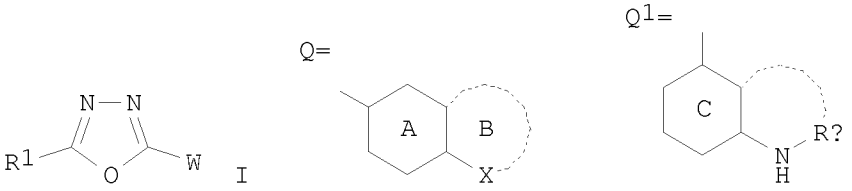


AB The title compds. [I; R1 = H, each (un)substituted hydrocarbyl, heterocyclyl, alkanoyl, HO, NH2, sulfonyl, sulfinyl, or SH, excluding diazacycloalkyl; W = Q, Q1; ring A = 6-membered aromatic ring; X = C, N, O, or S atom; ring B = 5- to 6-membered heterocyclic ring optionally having substituents at any position except X and optionally containing 1-3 N atom(s) or one S or N atom; ring C = (un)substituted N-containing 6-membered aromatic ring; Rw = H, acyl, each (un)substituted hydrocarbyl or heterocyclyl; or Rw together with the adjacent NH and the C atoms on the ring C form (un)substituted N-containing 5- to 7-membered ring] or salts thereof or prodrugs thereof are prepared These compds. are GSK-3β inhibitors, promoters of neural stem cell differentiation, and agents for lowering blood sugar (hypoglycemics) and useful as prophylactic/therapeutic agents for a GSK-3β-related condition or disease including neurodegenerative diseases, Alzheimer's disease, or diabetes. Thus, a suspension of 5-(benzothiazol-6-yl)-1,3,4-oxadiazol-2-thiol, 4-methoxy-3-(trifluoromethyl)benzyl bromide, and K2CO3 in DMF was stirred at room temperature for 5 h to give 6-[5-[[4-methoxy-3-(trifluoromethyl)benzyl]thio]-1,3,4-oxadiazol-2-yl]benzothiazole (II). 2-(1,3-Benzodioxol-5-yl)-5-[(3-fluoro-4-methoxybenzyl)thio]-1,3,4-oxadiazole (com. available compound), 2-[3-(4-methoxyphenyl)benzofuran-5-yl]-5-(methylthio)-1,3,4-oxadiazole, and 4-[5-[(3-fluoro-4-methoxybenzyl)thio]-1,3,4-oxadiazol-2-yl]pyridine-2-amine showed IC50 of 0.065, 0.19, and 0.14 μM against GSK-3β, resp., and did not show IC50 of 10 μM against other various kinases, i.e. serine. threonine kinases (e.g. p38α, JNK1, IKKβ, ASK1, TAK1, MEKK1, PKC0). Pharmaceutical formulations, e.g. a tablet formulation containing II, were prepared

RE.CNT 230 THERE ARE 230 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:934797 CAPLUS
DN 147:301186
TI Preparation of imidazo[1,2-a]pyridines and imidazo[1,2-b]pyridazines as PI-3 kinase inhibitors
IN Ni, Zhi-Jie; Pecchi, Sabina; Burger, Matthew; Han, Wooseok; Smith, Aaron; Atallah, Gordana; Bartulis, Sarah; Frazier, Kelly; Verhagen, Joelle; Zhang, Yanchen; Iwanowicz, Ed; Hendrickson, Tom; Knapp, Mark; Merritt, Hanne; Voliva, Charles; Wiesmann, Marion; Legrand, Darren Mark; Bruce, Ian; Dale, James; Lan, Jiong; Levine, Barry; Costales, Abran; Liu, Jie; Pick, Teresa; Menezes, Daniel
PA Novartis A.-G., Switz.
SO PCT Int. Appl., 236pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007095588	A1	20070823	WO 2007-US62157	20070214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

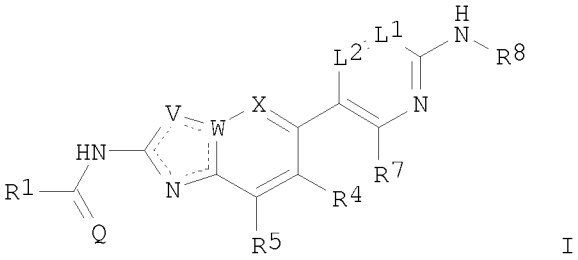
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-773476P P 20060214

US 2006-876729P P 20061222

OS MARPAT 147:301186

GI



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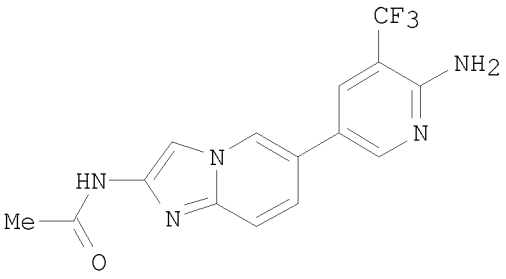

II

AB Title compds. represented by the formula I [wherein Q = O or S; X = CR3 or N; W = C or N; V = CR2, O or S; L1 = CR9 or N; L2 = CR6 or N; R1 = H, (un)substituted alkyl alkenyl, etc.; R2, R3, R7, R9 = independently H, (un)substituted alkyl, (hetero)aryl, etc.; R4-R6 = independently H, halo, cyano, etc.; R8 = H, (un)substituted alkyl, heterocyclyl, etc.; and stereoisomers, tautomers, or pharmaceutically acceptable salts thereof] were prepared as Phosphatidylinositol 3 (PI-3) kinase inhibitor. For example, reaction of N-(6-iodoimidazo[1,2-a]pyridin-2-yl)acetamide with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(trifluoromethyl)pyridin-2-amine gave II•TFA in 21% yield. I showed PI3K inhibitory with IC50 value of less than about 10 μM. Thus, I and their pharmaceutical compns. are useful for the prophylaxis or treatment of proliferative diseases characterized by the abnormal activity of growth factors, protein serine/threonine kinases, phospholipid kinases, G-protein coupled receptors, and phosphatases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:730670 CAPLUS

DN 147:143405

TI Preparation of pyrrolo[2,3-b]pyridines as inhibitors of Akt activity

IN Seefeld, Mark Andrew; Hamajima, Toshihiro; Jung, David Kendall; Nakamura, Hiroko; Reid, Paul R.; Reno, Michael John; Rouse, Meagan B.; Heerding, Dirk A.; Tang, Jun; Wang, Jizhou

PA Smithkline Beecham Corporation, USA

SO PCT Int. Appl., 273pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007076423	A2	20070705	WO 2006-US62453	20061221
WO 2007076423	A3	20071129		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI US 2005-753033P P 20051222

US 2006-793198P P 20060419

OS MARPAT 147:143405

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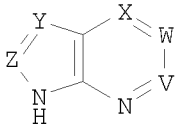

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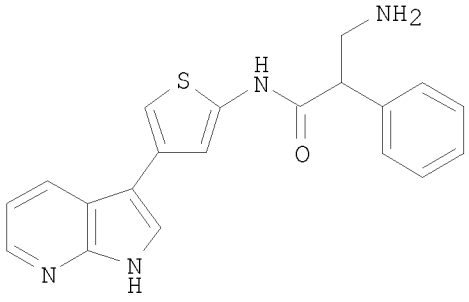


II

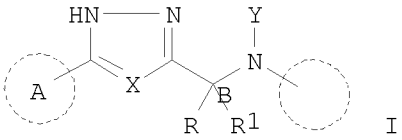
AB Title compds. represented by the formula I [wherein V = CH or N; Z = CR7 or N; R7 = H, CO2H, CO2-alkyl or alkyl; W, X, Y = independently CR5, CR10 or N; R5 = H, alkyl, aryl, etc.; R10 = substituted thienyl; and pharmaceutically acceptable salts, hydrates, solvates or prodrugs thereof] were prepared as Akt inhibitors. For example, II was provided in a multi-step synthesis starting from the reaction of 3-iodo-1H-pyrrolo[2,3-b]pyridine with benzenesulfonyl chloride.
Some of prepared compds. were tested in the Akt enzyme assay and each exhibited an IC50 value less than or equal to 0.5 μM against Akt1, Akt2 and Akt3. Thus, I and their pharmaceutical compns. are useful as inhibitors of protein kinase B activity and in the treatment of cancer and arthritis.

L2 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:505118 CAPLUS
DN 146:482074
TI Preparation of azole heterocyclic compounds as G protein-coupled receptor kinase (GRK) inhibitors
IN Kawamoto, Tetsuji; Okawa, Tomohiro; Hosono, Hiroshi; Ogino, Masaki
PA Takeda Chemical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 175pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2007112789	A	20070510	JP 2006-249474	20060914
PRAI JP 2005-276722	A	20050922		

OS MARPAT 146:482074
GI



I

AB The title compds. [I; R = each (un)substituted amino-lower alkyl, N-containing heterocyclyl-lower alkyl, or N-containing heterocyclyl; R1 = H, lower alkyl, each (un)substituted amino-lower alkyl, N-containing heterocyclyl-lower alkyl, or N-containing heterocyclyl; or R and R1 are bonded to each other to form a N-containing heterocyclic ring; ring A = (un)substituted N-containing heterocyclic ring; ring B = (un)substituted aromatic ring; X = N, C-R2; R2 = H, halo, each (un)substituted hydrocarbyl, heterocyclyl, NH2, HO, or CONH2, NO2, cyano, optionally esterified CO2H, acyl; Y = H, each (un)substituted hydrocarbyl, heterocyclyl, or CONH2, optionally esterified CO2H, acyl] or salts thereof are prepared These compds. are useful as preventive and therapeutic agents of circulatory diseases such as heart failure, hypertension, and arteriosclerosis, etc., based on the potent GRK inhibitory action. Thus, (2S)-2-phenylamino-4-[(tert-butoxycarbonyl)amino]butanoic acid hydrazide underwent cycloaddn. reaction with 4-cyanopyridine NaOEt in ethanol at 95° for 15 h to give 3-[(tert-Butoxycarbonyl)amino]-1-phenylamino-1-[3-(4-pyridyl)-1H-1,2,4-triazol-5-yl]propane which was stirred in concentrated HCl at room temperature for 30 min to give 3-amino-1-phenylamino-1-[3-(4-pyridyl)-1H-1,2,4-triazol-5-yl]propane trihydrochloride (II). II in vitro inhibited the GRK2-dependent phosphorylation of bovine tubulin with IC50 of ≤250 μM. II and 2-amino-1-(3-chlorophenyl)amino-1-[3-(4-pyridyl)-1H-1,2,4-triazol-5-yl]ethane trihydrochloride promoted the accumulation of cAMP in HEK293 cells overexpressing human β2 receptor with EC50 of 3.0 and 0.58 μM, resp. Pharmaceutical formulations, e.g. a capsule containing II, were prepared

L2 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1157352 CAPLUS
DN 145:471547
TI Preparation of morpholinobenzothiazoles and related compounds as phosphoinositide 3 kinase (PI3K) inhibitors
IN Alexander, Rikki Peter; Aujla, Pavandeep; Batchelor, Mark James; Brookings, Daniel Christopher; Buckley, George Martin; Crepy, Karen Viviane Lucile; Kulisa, Claire Louise; Turner, James Petrie

PA UCB S. A., Belg.
SO PCT Int. Appl., 144pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006114606	A1	20061102	WO 2006-GB1505	20060425
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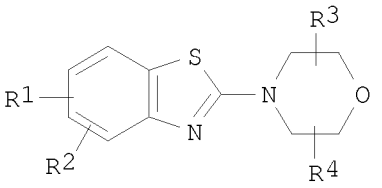
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006239018	A1	20061102	AU 2006-239018	20060425
CA 2607426	A1	20061102	CA 2006-2607426	20060425
EP 1881827	A1	20080130	EP 2006-726894	20060425
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
PRAI GB 2005-8471	A	20050426		
WO 2006-GB1505	W	20060425		

OS MARPAT 145:471547
GI



I

AB Title compds. [I; X = CO, CS, C(:NOR5), CH(OH), NR5CO, NR6CS, C(:NNH2); R1, R2 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl heterocycloalkyl heterocyclylalkyl, heteroaryl, heteroarylalkyl; R1R2, R3R4 = atoms to form rings; R3, R4 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, aralkynyl, biarylalkyl, heterocycloalkyl, heteroaryl, heteroarylarylalkyl, arylheteroarylalkyl, etc.; R5, R6 = H, alkyl], were prepared Thus, spiro[4,5]decane-7,9-dione in HOAc was treated dropwise with Br2 to give a crude product which was heated with morpholine-4-carbothioamide (preparation given) and diisopropylethylamine in THF to give 2% 2-(morpholin-4-yl)-4H-spiro[1,3-benzothiazole-5,1'-cyclopentan]-7(6H)-one. I showed binding affinity of ≤50 μM for human PI3K isoforms.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:735123 CAPLUS
DN 146:223251

TI A General Strategy for Creating "Inactive-Conformation" Abl Inhibitors
AU Okram, Barun; Nagle, Advait; Adrian, Francisco J.; Lee, Christian; Ren, Pingda; Wang, Xia; Sim, Taebo; Xie, Yongping; Wang, Xing; Xia, Gang; Spraggon, Glen; Warmuth, Markus; Liu, Yi; Gray, Nathanael S.
CS Department of Chemistry and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Chemistry & Biology (Cambridge, MA, United States) (2006), 13(7), 779-786
CODEN: CBOLE2; ISSN: 1074-5521
PB Cell Press
DT Journal
LA English
AB Summary: Kinase inhibitors that bind to the ATP cleft can be broadly classified into two groups: Those that bind exclusively to the ATP site with the kinase assuming a conformation otherwise conducive to phosphotransfer (type I), and those that exploit a hydrophobic site immediately adjacent to the ATP pocket made accessible by a conformational rearrangement of the activation loop (type II). To date, all type II inhibitors were discovered by using structure-activity-guided optimization strategies. Here, we describe a general pharmacophore model of type II inhibition that enables a rational "hybrid-design" approach whereby a 3-trifluoromethylbenzamide functionality is appended to four distinct type I scaffolds in order to convert them into their corresponding type II counterparts. We demonstrate that the designed compds. function as type II inhibitors by using biochem. and cellular kinase assays and by cocrystallog. with Abl.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:677905 CAPLUS
DN 145:145735
TI Preparation of pyrazinamines and pyridinamines which bind to the active site of protein kinase enzymes
IN Birault, Veronique; Harris, Clifford John; Crossley, Roger
PA Biofocus Discovery Limited, UK
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006072792	A2	20060713	WO 2006-GB34	20060106
	WO 2006072792	A3	20070111		

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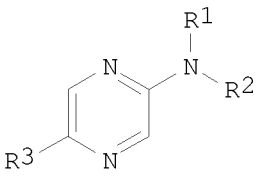
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI GB 2005-226 A 20050107
OS MARPAT 145:145735
GI



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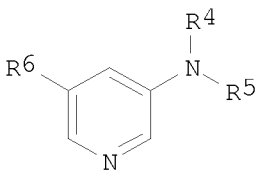

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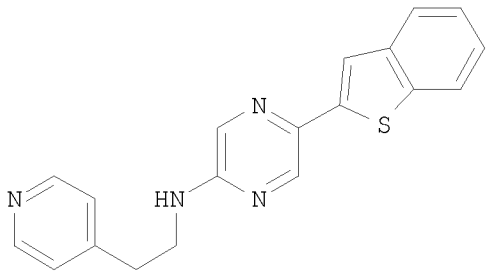


III

AB One or more compds. I and II [NR1R2 = ring; or R1 = H, and R2 = (un)substituted benzyl, 2-(pyridin-4-yl)ethyl, benzo[1,3]dioxol-4-ylmethyl, etc.; R3 = benzofuran-2-yl, naphthalen-2-yl, etc.; NR4R5 = ring; or R4 = H, and R5 = 3-hydroxyphenyl, 3-hydroxybenzoyl, (un)substituted benzyl, etc.; R6 = 3-carbamoylphenyl, 4-hydroxyphenyl, 1H-indol-5-yl, etc.] that are inhibitors of a serine/threonine kinase, more particularly Rho kinase (ROK, ROCK) can be used in the manufacture of a medicament for treatment or prophylaxis of a condition selected from: an ocular condition including age related macular degeneration, lacrimal gland disease or diabetic retinopathy, or suppression of neurite growth and hence a condition requiring nerve cell extension and connectivity, neuronal regeneration, inducing new axonal growth and promotion of axonal (re)wiring, repairing damage to neurons in the CNS caused by trauma (e.g., stroke, traumatic brain injury, etc.) or neurodegeneration (e.g., Alzheimer's, Parkinson's, etc.), repair and recovery from and treatment of disorders such as spinal cord injury and in reducing the subsequent effects thereof, or pain caused by nerve cell damage such as following trauma or amputation for example in the treatment of neuropathic pain. Over 100 compds. I and II were prepared E.g., a 2-step synthesis of III, starting from 2,5-dibromopyrazine and 2-(pyridine-4-yl)ethylamine, was given. Compds. I and II were tested against ROK kinase (data given).

L2 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:608573 CAPLUS
DN 145:103647
TI Preparation of naphthyridine derivatives as inhibitors of Akt activity
IN Arruda, Jeannie M.; Campbell, Brian T.; Cosford, Nicholas D. P.; Hoffman, Jacob M.; Hu, Essa H.; Layton, Mark E.; Li, Yiwei; Liang, Jun; Rodzinak, Kevin J.; Siu, Tony; Stearns, Brian A.; Tehrani, Lida R.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

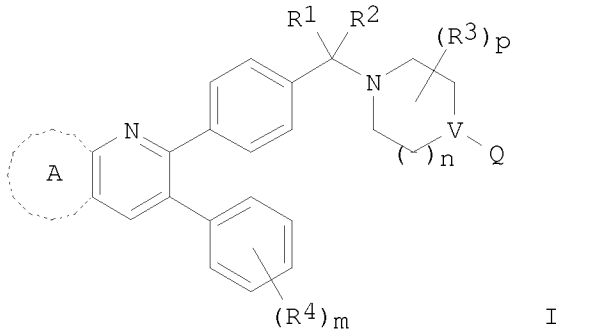
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006065601	A2	20061019	WO 2005-US44294	20051209
	WO 2006065601	A3	20070809		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

AU 2005316826	A1	20060622	AU 2005-316826	20051209
CA 2589084	A1	20060622	CA 2005-2589084	20051209
EP 1827436	A2	20070905	EP 2005-853256	20051209
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
IN 2007DN04504	A	20070831	IN 2007-DN4504	20070613
PRAI US 2004-636203P	P	20041215		
WO 2005-US44294	W	20051209		

OS MARPAT 145:103647

GI



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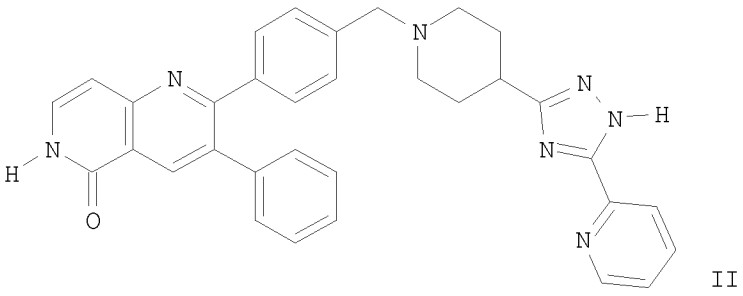

II

AB Title compds. I [Ring A forms a fused substituted 6-membered ring containing N; R1 and R2 independently = H, alkyl, perfluoroalkyl or combined to form a carbocycle or heterocycle; R3 independently = halo, alkyl, hydroxyalkyl, etc.; R4 independently = halo, oxo, OH , CN, etc.; m = 0-4; n = 0-1; p = 0-4; Q = aryl, arylcarbonyl, heterocycle, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as having the ability to inhibit the activity of Akt, a serine/ threonine protein kinase. Thus, e.g., II was prepared via

reductive amination of 4-(5-methoxy-3-phenyl-1,6-naphthyridin-2-yl)benzaldehyde (preparation given) with 2-(3-piperidin-4-yl-1H-1,2,4-triazol-5-yl)pyridine dihydrochloride (preparation given) followed by demethylation. In described assays for Akt kinase inhibition, specific compds. of the invention were tested and found to have IC50 values of ≤ 50 μM against one or more of Akt1, Akt2 and Akt3. The invention is further directed to chemotherapeutic compns. containing the compds. of this invention and methods for treating cancer comprising administration of the compds. of the invention. These substituted naphthyridines have unexpected advantageous properties when compared to other naphthyridines reported in PCT publication WO2003/086394, such unexpected advantageous properties may include increased cellular potency/solubility, greater selectivity, enhanced pharmacokinetic properties, lack of off target activity, etc.

L2 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:318893 CAPLUS
DN 144:370118
TI Preparation of pyrido[2,3-d]pyrimidine derivatives as inhibitors of Akt activity for treatment of cancer
IN Bilodeau, Mark T.; Cosford, Nicholas D. P.; Hartnett, John C.; Liang, Jun; Manley, Peter J.; Neilson, Lou Anne; Siu, Tony; Wu, Zhicai; Li, Yiwei
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006036395	A2	20060406	WO 2005-US29941	20050819
	WO 2006036395	A3	20071221		
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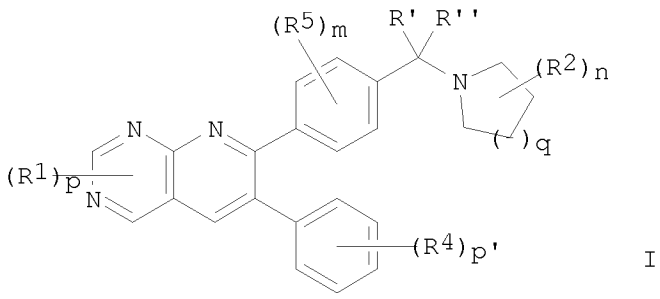
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	AU 2005290081	A1	20060406	AU 2005-290081	20050819
	CA 2576172	A1	20060406	CA 2005-2576172	20050819
	EP 1784175	A2	20070516	EP 2005-807835	20050819
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	JP 2008510823	T	20080410	JP 2007-530047	20050819
	US 20070254901	A1	20071101	US 2007-659606	20070206
	IN 2007DN02189	A	20070803	IN 2007-DN2189	20070321
PRAI	US 2004-603728P	P	20040823		
	WO 2005-US29941	W	20050819		

OS CASREACT 144:370118; MARPAT 144:370118
GI



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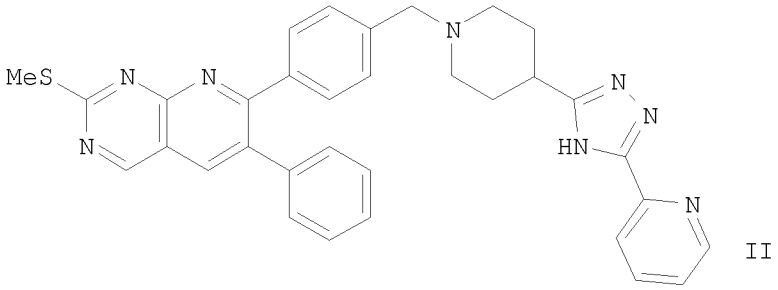
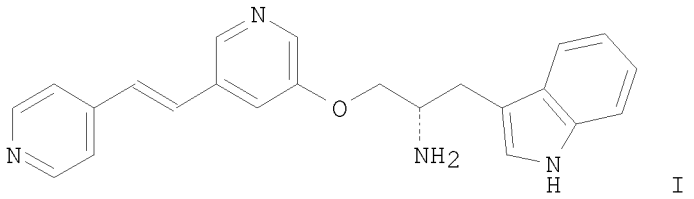


II

AB The title compds. I [wherein m = 0-4; n = 0-5; p = 0-3; q = 0-4; p' = 0-5; R1 = halo, oxo, OH, CN, etc.; R2, R4, and R5 = independently CN, CF3, NO2, etc.; R' and R'' = independently H, alkyl, or perfluoroalkyl; or R' and R'' form a ring; with provisos] or pharmaceutically acceptable salts or stereoisomers thereof were prepared as inhibitors of the activity of Akt, which is a serine/threonine protein kinase. For example, the compound II was prepared in a multi-step synthesis. I are useful for the treatment of cancer (no data).

L2 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:128521 CAPLUS
DN 144:390708
TI Discovery of trans-3,4'-bispyridinylethylenes as potent and novel inhibitors of protein kinase B (PKB/Akt) for the treatment of cancer: Synthesis and biological evaluation
AU Li, Qun; Li, Tongmei; Zhu, Gui-Dong; Gong, Jianchun; Claibone, Akiyo; Dalton, Chris; Luo, Yan; Johnson, Eric F.; Shi, Yan; Liu, Xuesong; Klinghofer, Vered; Bauch, Joy L.; Marsh, Kennan C.; Bouska, Jennifer J.; Arries, Shannon; De Jong, Ron; Oltersdorf, Tilman; Stoll, Vincent S.; Jakob, Clarissa G.; Rosenberg, Saul H.; Giranda, Vincent L.
CS Cancer Research, GPRD, Abbott Laboratories, Abbott Park, IL, 60064-6101, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(6), 1679-1685
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:390708
GI



I

AB Pyridinylethenylpyridinyloxyethylamines such as I, pyridinylethenylpyridinylaminoethylamines, pyridinylethenylpyridineethylamines, and pyridinylethenylpyridinyloxypropylamines are prepared as Akt/PKB inhibitors for the treatment of cancer; I inhibits Akt1 with an IC50 value of 14 nM. I is highly selective for Akt1 over kinases from other kinase families such as tyrosine kinases and calmodulin-dependent protein kinases, and is poorly to modestly selective for Akt1 over closely related kinases in the protein kinase A, G, and C family and over kinases in the CMGC group. The pharmacokinetics of I and of other pyridinylethenylpyridine derivs. are determined in mice, rats, dogs, and/or monkeys. The structure of I complexed with protein kinase A in its ATP binding site is determined by x-ray crystallog.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1240986 CAPLUS
DN 144:22906
TI Preparation of fused heterocycle kinase inhibitors for treatment of protein tyrosine kinase-related diseases
IN Cusack, Kevin; Salmeron-Garcia, Jose-Andres; Gordon, Thomas D.; Barberis, Claude E.; Allen, Hamish J.; Bischoff, Agniezka K.; Ericsson, Anna M.; Friedman, Michael M.; George, Dawn M.; Roth, Gregory P.; Talanian, Robert V.; Thomas, Christine; Wallace, Grier A.; Wishart, Neil; Yu, Zhengtian
PA Abbott Laboratories, USA
SO PCT Int. Appl., 362 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005110410	A2	20051124	WO 2005-US16903	20050513
	WO 2005110410	A3	20070329		
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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2566158	A1	20051124	CA 2005-2566158	20050513
	US 20060074102	A1	20060406	US 2005-129624	20050513
	EP 1753428	A2	20070221	EP 2005-778736	20050513
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA,				

HR, LV, MK, YU

	JP 2007537296	T	20071220	JP 2007-513433	20050513
	MX 2006PA13250	A	20070228	MX 2006-PA13250	20061114
PRAI	US 2004-571281P	P	20040514		
	WO 2005-US16903	W	20050513		

OS MARPAT 144:22906

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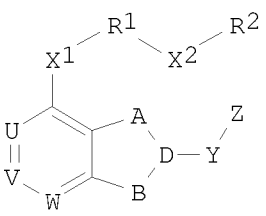

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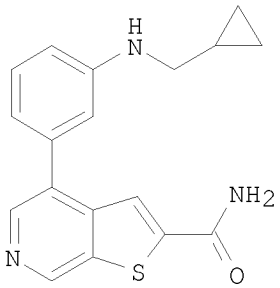


II

AB The invention is related to the preparation of fused heterocycles of formula I [A, B = independently N, S, O, a bond, etc.; D = C, N, S, O, C:C; U, V, W = independently CH and derivs., N; Y = a bond, CONH2 and derivs., SO, etc.; Z = H, halo, CN, etc.; X1 = a bond, halo, O, SO, NHSO2, etc.; R1 = a bond, (un)substituted benzofuranyl, benzimidazolyl, pyrrolyl, etc.; when R1 is not a bond, then X2 = a bond, O,S, NHCO and derivs., aliphatic group, etc.; or when R1 = a bond, then X2 = a bond and R2 is not a bond; R2 = a bond or (un)substituted benzoxazolyl, Ph, etc.; with provisos; and with the exception of certain compds.], and their pharmaceutically acceptable salts as inhibitors of kinases, particularly COT or MK2 kinases. The invention is also related to the use of certain compds. I as inhibitors of angiogenic receptor tyrosine kinases. Thus, reacting 4-(3-aminophenyl)thieno[2,3-c]pyridine-2-carboxamide with cyclopropanecarboxaldehyde gave thienopyridine II. All compds. I significantly inhibit either COT or MK2 at concns. of 50 μM or below.

L2 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:177838 CAPLUS

DN 142:280057

TI Preparation of substituted pyridinones as modulators of p38 MAP kinase

IN Devadas, Balekudru; Walker, John; Selness, Shaun R.; Boehm, Terri L.; Durley, Richard C.; Devraj, Rajesh; Hickory, Brian S.; Rucker, Paul V.; Jerome, Kevin D.; Madsen, Heather M.; Alvira, Edgardo; Promo, Michele A.; Blevis-Bal, Radhika M.; Marrufo, Laura D.; Hitchcock, Jeff; Owen, Thomas; Naing, Win; Xing, Li; Shieh, Huey S.; Sambandam, Aruna; Liu, Shuang; Scott, Ian L.; Mcgee, Kevin F.

PA Pharmacia Corporation, USA

SO PCT Int. Appl., 968 pp.
CODEN: PIXXD2

DT Patent

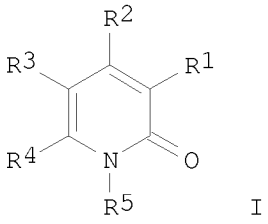
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005018557	A2	20050303	WO 2004-US26193	20040813
	WO 2005018557	A3	20050804		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
NL 1026826 A1 20050216 NL 2004-1026826 20040812
NL 1026826 C2 20070104
US 20050176775 A1 20050811 US 2004-918826 20040813
PRAI US 2003-494959P P 20030813
OS MARPAT 142:280057
GI



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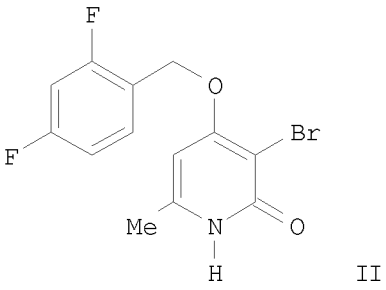

II

AB Disclosed are title compds. I and their pharmaceutically acceptable salts [R1 H, halo, NO2, CHO, CN, (un)substituted hydroxy/dihydroxy/aryl/alkyl, etc.; R2 = H, OH, halo, (un)substituted alkyl, alkoxy, etc.; R3 = H, halo, (un)substituted aryl/alkoxycarbonyl, arylalkyl, arylthio, etc.; R4 = H, (un)substituted alkyl; R5 = H, aryl, arylalkyl, etc.]. These compds. are useful for treating diseases and conditions caused or exacerbated by unregulated p38 MAP Kinase and/or TNF activity. Pharmaceutical compns. containing the compds., methods of preparing the compds. and methods of treatment
using the compds. are also disclosed. For example, II was prepared, in 3 steps, reacting 4-hydroxy-6-methylpyrone with NH4OH, followed by O-alkylation with 2,4-difluorobenzyl chloride, and bromination with Br2 in AcOH/H2O. Selected I inhibited MKK6-activated human p38α kinase phosphorylation of a biotinylated substrate or human p38α-induced

phosphorylation of EGFRP (epidermal growth factor receptor peptide) with an IC50 in the range of 1 μM to 25 μM.

L2 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:182868 CAPLUS
DN 140:235595
TI Preparation of pyrrole based selective inhibitors of glycogen synthase kinase 3 for treating diabetes and other disorders
IN Desai, Manoj; Ni, Zhi-Jie; Ng, Simon; Pfister, Keith B.; Ramurthy, Savithri; Subramanian, Sharadha; Wagman, Allan S.
PA Chiron Corporation, USA
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004018455	A1	20040304	WO 2003-US26625	20030821
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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	CA 2496246	A1	20040304	CA 2003-2496246	20030821
	AU 2003268184	A1	20040311	AU 2003-268184	20030821
	US 20040077707	A1	20040422	US 2003-646625	20030821
	US 7250443	B2	20070731		
	EP 1537099	A1	20050608	EP 2003-749133	20030821
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	CN 1688573	A	20051026	CN 2003-824335	20030821
	JP 2006501243	T	20060112	JP 2004-531200	20030821
	IN 2005KN00471	A	20060203	IN 2005-KN471	20050321
	US 20070244109	A1	20071018	US 2007-761937	20070612
PRAI	US 2002-405846P	P	20020823		
	US 2003-646625	A3	20030821		
	WO 2003-US26625	W	20030821		

OS MARPAT 140:235595
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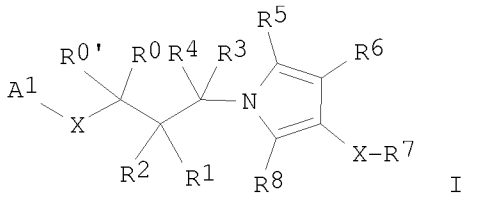

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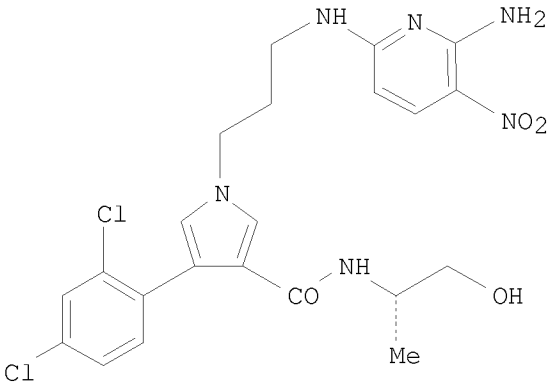


II

AB New pyrrole based compds. (shown as I; variables defined below; e.g. II), compns. and methods of inhibiting the activity of glycogen synthase kinase (GSK3) in vitro and of treatment of GSK3 mediated disorders in vivo are provided. The methods, compds. and compns. of the invention may be employed alone, or in combination with other pharmacol. active agents in the treatment of disorders mediated by GSK3 activity, such as diabetes, Alzheimer's disease and other neurodegenerative disorders, obesity, atherosclerotic cardiovascular disease, essential hypertension, polycystic ovary syndrome, syndrome X, ischemia, traumatic brain injury, bipolar disorder, immunodeficiency or cancer. For I: X is N, O, or (un)substituted C; W is absent or -O-, -S-, -S(O)-, -SO2-, -NH-, -NH-CO-, -NR'CO-, -NHSO2-, -NR'SO2-, -CO-, -CO2-, -CH2-, -CF2-, -CHF-, -CONH-, -CONR'-, and -NR'-, where R' is (un)substituted alkyl, cycloalkyl, aryl, heteroaryl, heterocyclo; A1 is (un)substituted aryl or heteroaryl; R0 and R0' = H and Me. R1, R2, R3, and R4 = H, hydroxy, and (un)substituted loweralkyl, cycloloweralkyl, cyclicaminoalkyl, alkylaminoalkyl, loweralkoxy, amino, alkylamino, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, aryl and heteroaryl. R5 and R8 = H, halo, and (un)substituted loweralkyl, cycloalkyl, alkoxy, amino, aminoalkoxy, carbonyloxy, aminocarbonyloxy, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, heteroaralkylcarbonylamino, cycloimido, heterocycloimido, amidino, cycloamidino, heterocycloamidino, guanidinyl, aryl, biaryl, heteroaryl, heteroarylaryl, heteroarylheteroaryl, heterocycloalkyl, heterocyclocarbonyloxy, heteroarylcarbonyloxy, and arylsulfonamido. R6 = H, and (un)substituted aryl, heteroaryl, and heterocyclo; R7 = H, hydroxy, halo, carboxy, nitro, amino, amido, amidino, imido, cyano, sulfonyl, methanesulfonyl, and (un)substituted alkyl, alkoxy, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, etc.; addnl. details are given in the claims. Although the methods of preparation are not claimed, example prepns. and characterization data are included for hundreds of I. For example, II was prepared in 7 steps starting with esterification of (E)-3-(2,4-dichlorophenyl)-2-propenoic acid with tBuOH, followed by cyclization with p-tolylSO2CH2NC to give 4-(2,4-dichlorophenyl)pyrrole-3-carboxylic acid

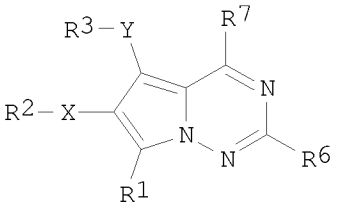
tert-Bu ester, followed by N-alkylation with 3-bromopropylphthalimide, followed by conversion of the phthalimide to the diamine with hydrazine, followed by N-substitution with (6-chloro-3-nitro-2-pyridyl)amine to give 1-[3-[(6-amino-5-nitropyridin-2-yl)amino]propyl]-4-(2,4-dichlorophenyl)pyrrole-3-carboxylic acid tert-Bu ester, followed by acid hydrolysis and carboxamide formation with (2S)-(+)-2-aminopropan-1-ol to give II. Representative I have GSK3 inhibitory activity <10 μM (specific compds. not mentioned); they exhibit a selectivity of ≥2-fold for GSK3 as compared to another kinase and more typically they exhibit a selectivity of ≥5-fold. Compds. I were shown to be capable of significantly reducing the potential of glutamate to induce neuronal cell death. In the glucose tolerance test, representative I exhibited good in vitro potency, and when formulated in captisol and administered s.c. to mice (30 mg/kg), exhibited high bioavailability and tissue penetrance in vivo. A significant reduction in basal hyperglycemia just prior to the glucose tolerance test, and significantly improved glucose disposal following glucose challenge were observed, comparable to the efficacy obtained with Troglitazone. Also of significance was the observation that insulin levels in treated animals remained lower than in control mice.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:120859 CAPLUS
DN 140:181471
TI Preparation of pyrrolotriazines as tyrosine kinase activity inhibitors of growth factor receptors for the treatment of cancer
IN Bhide, Rajeev S.; Borzilleri, Robert M.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004013145	A1	20040212	WO 2003-US24273	20030804
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003265349	A1	20040223	AU 2003-265349	20030804
	US 20040063708	A1	20040401	US 2003-633997	20030804
	US 6951859	B2	20051004		
	EP 1543009	A1	20050622	EP 2003-767116	20030804
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 20050234060	A1	20051020	US 2005-157890	20050621
PRAI	US 2002-400572P	P	20020802		
	US 2003-633997	A3	20030804		
	WO 2003-US24273	W	20030804		

OS MARPAT 140:181471
GI



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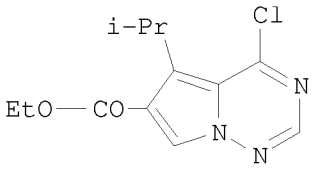
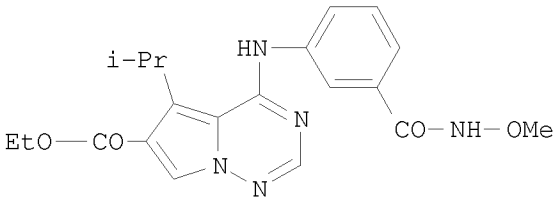


II



III

AB Title compds. I [R7 = ZR41R42; Z = O, S, N, OH, Cl with the provisos that when Z is O or S, R41 is absent and when Z is OH or Cl, both R41 and R42 are absent and when Z is N, then R41 is H; X, Y = O, OCO, S, etc.; R1 = H, CH3, OH, etc.; R2, R3 = H, (un)substituted alkyl, alkenyl, etc.; R6 = H, (un)substituted alkyl, aryl, etc.; R42 = (un)substituted N-alkoxybenamides] and their pharmaceutically acceptable salts were prepared For example, condensation of 3-methoxyaminocarbonylaniline and chloropyrrolotriazine II, e.g., prepared from Et isocyanoacetate in 4-steps, afforded claimed pyrrolotriazine III in 65% yield. Compds. I in VEGFR-2 and FGFR-1 kinases inhibition assays exhibited IC50 values ranging from 0.01-10 μM. Of note, compds. I are selective inhibitors of VEGFR-2 and FGFR-1 kinase enzymes and min. activity against CDK-2 kinase and LCK and Src kinases. Compds. I are claimed useful for the treatment of diseases associated with signal transduction pathways operating through growth factor receptors.

L2 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:80698 CAPLUS
DN 140:146173
TI Preparation of pyrrolotriazines as selective VEGFR-2 and FGFR-1 kinase inhibitors for treatment of proliferative diseases
IN Bhide, Rajeev; Ruel, Rejean; Thibeault, Carl; L'heureux, Alexandre
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004009601	A1	20040129	WO 2003-US22554	20030718

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA	2492665	A1	20040129	CA 2003-2492665	20030718
AU	2003254017	A1	20040209	AU 2003-254017	20030718
US	20040063707	A1	20040401	US 2003-622593	20030718
US	6969717	B2	20051129		
US	20040072832	A1	20040415	US 2003-623171	20030718
US	6869952	B2	20050322		
EP	1539763	A1	20050615	EP 2003-765754	20030718

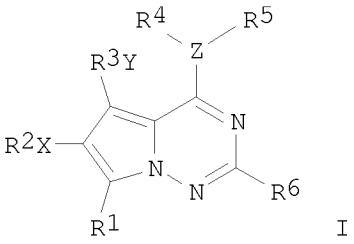
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

CN	1681818	A	20051012	CN 2003-821820	20030718
CN	1681508	A	20051012	CN 2003-821915	20030718
JP	2005538990	T	20051222	JP 2004-523591	20030718
BR	2003012801	A	20070626	BR 2003-12801	20030718
CN	1903840	A	20070131	CN 2006-10115789	20030721
US	20050124621	A1	20050609	US 2005-35248	20050113
US	7265113	B2	20070904		
MX	2005PA00716	A	20050408	MX 2005-PA716	20050117
ZA	2005000492	A	20060830	ZA 2005-492	20050118
ZA	2005000496	A	20060830	ZA 2005-496	20050118
NO	2005000417	A	20050217	NO 2005-417	20050125
US	20060058304	A1	20060316	US 2005-214267	20050829
US	20070299075	A1	20071227	US 2007-832976	20070802

PRAI	US 2002-397256P	P	20020719		
	US 2003-447213P	P	20030213		
	US 2003-622280	A	20030718		
	US 2003-622593	A3	20030718		
	US 2003-623171	A1	20030718		
	WO 2003-US22554	W	20030718		
	CN 2003-816201	A3	20030721		
	US 2005-35248	A1	20050113		

OS MARPAT 140:146173

GI



I

AB Title compds. I [Z = O, S, N, etc.; X, Y = O, OCO, S, etc.; R1 = H, CH3, OH, etc.; R2, R3 = H, (un)substituted alkyl, alkenyl etc.; R4 = (un)substituted 7-azaindolyl, e.g., F, Cl, Me; R5 = H, absent when Z = O, S; R6 = H, (un)substituted alkyl, aryl, etc.] and their pharmaceutically acceptable salts were prepared For example, electrophilic substitution of compound I [R1 = H; R2X = benzyloxy; R3Y = CH3; ZR5R6 = Cl] with 4-fluoro-5-hydroxy-7-azaindole, e.g., prepared from 4-chloro-1H-pyrrolo[2,3-b]pyridine in 6-steps, afforded compound I [R1 = H; R2X = benzyloxy; R3Y = CH3; ZR5R6 = 4-fluoro-7-azaindol-5-yloxy] in 80% yield. In VEGFR-2 and FGFR-1 kinase assays, 38-examples of compds. I exhibited IC50 values ranging from 0.001-10 μM. Of note, pyrrolotriazines I exhibited selective VEGFR-2 and FGFR-1 kinase inhibition (no data provided). Compds. I are claimed useful for the treatment of cancer, inflammation, autoimmune diseases.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:972071 CAPLUS
DN 140:27837
TI Preparation of 2-oxo-1,2,3,4-tetrahydroquinazolines as Cdk2 and Cdk5 kinase inhibitors for the treatment of cell proliferation-related disorders
IN Huang, Qi; Kaller, Matthew; Nguyen, Thomas; Norman, Mark H.; Rzasa, Robert; Wang, Hui-Ling; Zhong, Wenge
PA Amgen Inc., USA
SO PCT Int. Appl., 253 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003101985	A1	20031211	WO 2003-US16941	20030529
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 20030229068	A1	20031211	US 2003-446440	20030527
	US 7119111	B2	20061010		
	CA 2486530	A1	20031211	CA 2003-2486530	20030529
	AU 2003273579	A1	20031219	AU 2003-273579	20030529
	EP 1507776	A1	20050223	EP 2003-741829	20030529
	EP 1507776	B1	20070228		
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	JP 2005533039	T	20051104	JP 2004-509676	20030529
	AT 355287	T	20060315	AT 2003-741829	20030529
	ES 2282646	T3	20071016	ES 2003-741829	20030529
	MX 2004PA11579	A	20050307	MX 2004-PA11579	20041122
PRAI	US 2002-384265P	P	20020529		
	US 2003-446440	A1	20030527		
	WO 2003-US16941	W	20030529		

OS MARPAT 140:27837
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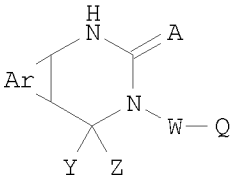

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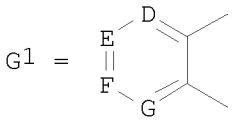
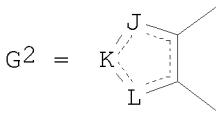
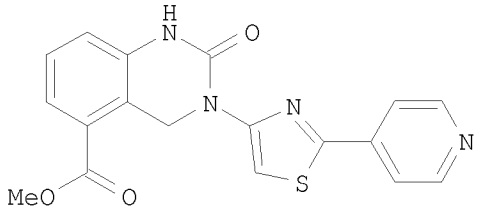






II

AB Title compds. I [wherein Ar = G1 or G2; A = O or S; D, E, F, and G = independently CR1, CR2, CR3, CR4, or N; J, K, and L = independently NR6, S, O, CR1, CR2, CR3, or CR4; Q = H, OH, N(R5)2, NR5COR5, (CH2)mOR5, (CH2)mSOnR5, NR5aSO2R5, or (un)substituted (hetero)aryl, carbocyclyl, or heterocyclyl; W = (un)substituted heterocyclyl; Y and Z = independently H, N(R5a)2, SR5a, OR5a, or C(R5a)3; m = 1-8; n = 0-2; R1, R2, R3, and R5 = independently H, OR5, alkylenedioxy, halo(alkyl), alkenyl, alkynyl, N(R5)2, (CH2)mN(R5)2, SOnN(R5)2, SOnR5, (hydroxy)alkyl, NO2, CN, COR5, NR5SO2R5, CON(R5)2, CO2R5, NR5CON(R5)2, NR5COR5, NR5CO2R5, or (un)substituted aryl(alkyl), cycloalkyl, or heterocyclyl(alkyl); or R1R2, R2R3, R3R4 may form carbocyclic or heterocyclic rings; R5 = independently H, (halo)alkyl, or (un)substituted aryl(alkyl), heterocyclyl(alkyl), cycloalkyl(alkyl), etc.; R5a and R6 = independently absent, H, or alkyl; with provisos; and pharmaceutically acceptable salts thereof] are disclosed as serine/threonine kinase inhibitors for effective treatment of cell proliferation or apoptosis-mediated diseases (no data). The invention encompasses I and pharmaceutically acceptable derivs. thereof, pharmaceutical compns., and methods for prophylaxis and treatment of diseases and other maladies or conditions involving stroke, cancer, and the like (no data). The invention also relates to processes for making such compds. as well as to intermediates useful in such processes. For example, II was prepared in five steps by bromination of Me 2-methyl-3-nitrobenzoate, coupling with prop-2-enyl N-[2-(4-pyridyl)-1,3-thiazol-4-yl]carbamate, reduction to the amine, deprotection, and cyclization using p-nitrophenyl chloroformate in the presence of DMAP (no data for intermediates). The quinazolinone II exhibited Cdk2/cyclin and Cdk5/p25 kinase activity with IC50 values < 1 μM and inhibited cell proliferation of human PC-3 prostate cells, HCT 116 human colon carcinoma cells, or HT 29 human colon carcinoma cells with IC50 < 5 μM.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:818232 CAPLUS
DN 139:323527
TI Preparation of triazolo[4,3-b]pyridazines and 2,3-diarylquinazolines for the treatment of cancer
IN Barnett, Stanley F.; Defeo-Jones, Deborah; Haskell, Kathleen M.; Huber,

Hans E.; Nahas, Deborah D.; Lindsley, Craig W.; Zhao, Zhijian; Hartman, George D.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 170 pp.
CODEN: PIXXD2

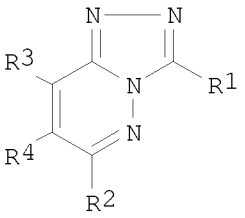
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003084473	A2	20031016	WO 2003-US10632	20030404
	WO 2003084473	A3	20040212		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003226301	A1	20031020	AU 2003-226301	20030404
	US 20060142178	A1	20060629	US 2004-510068	20041004
PRAI	US 2002-370827P	P	20020408		
	US 2002-417202P	P	20021009		
	WO 2003-US10632	W	20030404		

GI



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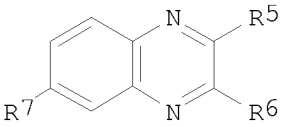


II

AB Triazolo[4,3-b]pyridazines I [R1 = (un)substituted Ph, furyl, thienyl, pyridinyl; R2 = substituted NH2, OH; R3 = H, R4 = (un)substituted cycloalkyl, aryl; R3R4 = (un)substituted CH:CHCH:CH] and quinazolines II [R5, R6 = (un)substituted Ph; R7 = H, alkyl, halogen, OH, alkoxy] were prepared for use as inhibitors of one or two of the isoforms of Akt, a serine/threonine protein kinase, acting particularly on the pleckstrin homol. domain of Akt. Thus, 3,6-dichloropyridazine was converted to its 4-cyclobutyl derivative which was cyclized with BzNHNH2 and aminated to give I [R1 = Ph, R2 = NHCH2CMe2CH2NMe2, R3 = H, R4 = cyclobutyl]. This compound had IC50 for inhibition of Akt1 of 1.4 μM.

L2 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:42265 CAPLUS

DN 138:106699

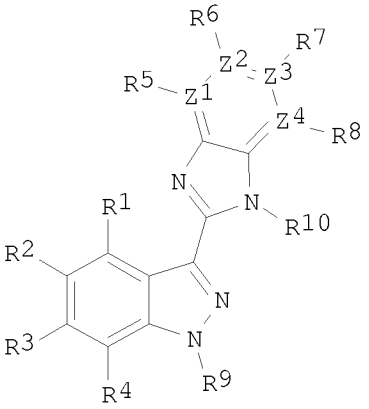
TI Preparation of (indazolyl)benzimidazoles and analogs as tyrosine and serine/threonine kinase inhibitors

IN Renhowe, Paul A.; Shafer, Cynthia M.; McBride, Chris; Silver, Joel; Pecchi, Sabina; Machajewski, Tim; Mccrea, Bill; Poon, Daniel; Thomas, Teresa

PA Chiron Corporation, USA
SO PCT Int. Appl., 435 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003004488	A1	20030116	WO 2002-US20844	20020702
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002354727	A1	20030121	AU 2002-354727	20020702
	EP 1401831	A1	20040331	EP 2002-752132	20020702
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2004536113	T	20041202	JP 2003-510655	20020702
PRAI	US 2001-302791P	P	20010703		
	WO 2002-US20844	W	20020702		

OS MARPAT 138:106699
GI



I

AB Title compds. I [wherein Z1-Z4 = C independently C or N; R1 = H, F, Cl, or Br; R2 = H, F, Cl, Br, CN, NO2, or (un)substituted CO2H, NH2, CONH2, NHCONH2, etc.; R3 = H, F, Cl, Br, or (un)substituted alkoxy; R4, R9, and R10 = H; R5 and R8 = independently H, F, Cl, or (un)substituted alkyl, alkoxy, NH2, heterocyclyl, etc.; R6 and R7 = independently H, F, Cl, Br, CF3, CO2H, or (un)substituted alkyl, (heterocyclyl)alkoxy, arylalkoxy, alkoxyalkoxy, (heterocyclyl)heterocyclyl, arylheterocyclyl, heterocyclyloxy, aryloxy, NH2, CONH2, etc.; or R5 is absent if Z1 = N; or R6 is absent if Z2 = N; or R7 is absent if Z3 = N; or R8 is absent if Z4 = N; with the proviso that at least one of R1, R2, R3, R5, R6, R7, or R8 ≠ H; and tautomers and pharmaceutically acceptable salts thereof] were prepared as tyrosine and serine/threonine kinase inhibitors. For example, dimerization of indazole-3-carboxylic acid with PO3 followed by addition of

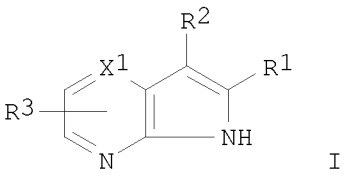
1,2-phenylenediamine in toluene gave 3-(1H-benzimidazol-2-yl)-1H-indazole. Seven hundred twenty-eight exemplary compds. were assays for serine/threonine kinase activity in vitro, and the majority displayed an IC50 value of less than 10 μM with respect to VEGFR1, Flk-1, bFGF, Tie-2, CHK-1, cdc2, GSK-3, NEK-2, and PDGF.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:5957 CAPLUS
DN 138:55984
TI Preparation of azaindoles as protein kinase inhibitors
IN Cox, Paul Joseph; Majid, Tahir Nadeem; Lai, Justine Yeun Quai; Morley, Andrew; Amendola, Shelley; Deprets, Stephanie Daniele; Edlin, Chris; Gardner, Charles J.; Kominos, Dorothea; Pedgrift, Brian Leslie; Halley, Frank; Gillespy, Timothy Alan; Edwards, Michael; Clerc, Francois Frederic; Nemecek, Conception; Houille, Olivier; Damour, Dominique; Bouchard, Herve; Bezard, Daniel; Carrez, Chantal
PA Aventis Pharma Limited, UK
SO PCT Int. Appl., 373 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003000688	A1	20030103	WO 2002-GB2799	20020620
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2451678	A1	20030103	CA 2002-2451678	20020620
	AU 2002302849	A1	20030108	AU 2002-302849	20020620
	EP 1397360	A1	20040317	EP 2002-730531	20020620
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	EE 200400015	A	20040415	EE 2004-15	20020620
	BR 2002010507	A	20040615	BR 2002-10507	20020620
	SI 21462	A	20041031	SI 2002-20015	20020620
	JP 2004534826	T	20041118	JP 2003-507091	20020620
	HU 2004000247	A2	20050128	HU 2004-247	20020620
	CN 1665809	A	20050907	CN 2002-812476	20020620
	NZ 529205	A	20060428	NZ 2002-529205	20020620
	AP 1739	A	20070630	AP 2003-2940	20020620
	NZ 545741	A	20070928	NZ 2002-545741	20020620
	SG 135051	A1	20070928	SG 2005-8069	20020620
	RU 2326880	C2	20080620	RU 2004-101408	20020620
	US 20040053931	A1	20040318	US 2002-177804	20020621
	US 6897207	B2	20050524		
	ZA 2003009648	A	20050311	ZA 2003-9648	20031211
	BG 108481	A	20050531	BG 2003-108481	20031219
	MX 2004PA00188	A	20040318	MX 2004-PA188	20040107
	US 20050267304	A1	20051201	US 2004-995103	20041123
PRAI	GB 2001-15109	A	20010621		
	US 2001-300257P	P	20010622		
	NZ 2002-529205	A3	20020620		

WO 2002-GB2799 W 20020620
US 2002-177804 A1 20020621
OS MARPAT 138:55984
GI



I

AB The invention is directed to physiol. active azaindoles (shown as I; variables defined below; e.g. 6-(5-methoxy-1-methyl-1H-indol-3-yl)-5H-pyrrolo[2,3-b]pyrazine) and compns. containing such compds.; and their prodrugs, and pharmaceutically acceptable salts and solvates of such compds. and their prodrugs. Such compds. and compns. have valuable pharmaceutical properties, in particular the ability to inhibit kinases, especially Syk, FAK, KDR, Aurora2 and IGF1R (data given in general rather than for specific I). Although the methods of preparation are not claimed, >100 example prepns. of intermediates and I are included. For I: R1 = aryl or heteroaryl each optionally substituted by ≥1 groups = alkylenedioxy, alkenyl, alkenyloxy, alkynyl, aryl, cyano, halo, hydroxy, heteroaryl, heterocycloalkyl, nitro, R4, -C(O)R, -C(O)OR5, -C(O)NY1Y2, -NY1Y2, -N(R6)C(O)R7, -N(R6)C(O)NY3Y4, -N(R6)C(O)OR7, -N(R6)SO2R7, -N(R6)SO2NY3Y4, -SO2NY1Y2 and -Z2R. R2 = H, acyl, cyano, halo, lower alkenyl, -Z2R4, -SO2NY3Y4, -NY1Y2 or lower alkyl optionally substituted by aryl, cyano, heteroaryl, heterocycloalkyl, hydroxy, -Z2R4, -C(O)NY1Y2, -C(O)R, -CO2R8, -NY3Y4, -N(R6)C(O)R, -N(R6)C(O)NY1Y2, -N(R6)C(O)OR7, -N(R6)SO2R7, -N(R6)SO2NY3Y4, -SO2NY1Y2 and ≥1 halogen atoms. R3 = H, aryl, cyano, halo, heteroaryl, lower alkyl, -Z2R4, -C(O)OR5 or -C(O)NY3Y4. R4 = alkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl or heterocycloalkylalkyl each optionally substituted by aryl, cycloalkyl, cyano, halo, heteroaryl, heterocycloalkyl, -CHO (or a 5- 6- or 7-membered cyclic acetal derivative thereof), -C(O)NY1Y2, -C(O)OR5, -NY1Y2, -N(R6)C(O)R7, -N(R6)C(O)NY3Y4, -N(R6)SO2R7, -N(R6)SO2NY3Y4, -Z3R7 and ≥1 hydroxy, alkoxy and carboxy. R5 = H, alkyl, alkenyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl. R6 = H or lower alkyl; R7 = alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl or heterocycloalkylalkyl; R8 = H or lower alkyl. R = aryl or heteroaryl; alkenyl; or alkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl or heterocycloalkylalkyl each optionally substituted by aryl, cycloalkyl, cyano, halo, heteroaryl, heterocycloalkyl, -CHO (or a 5- 6- or 7-membered cyclic acetal derivative thereof), -C(O)NY1Y2, -C(O)OR5, -NY1Y2, -N(R6)C(O)R7, -N(R6)C(O)NY3Y4, -N(R6)SO2R7, -N(R6)SO2NY3Y4, -Z3R7 and ≥1 hydroxy, alkoxy and carboxy. X1 = N, CH, C-aryl, C-heteroaryl, C-heterocycloalkyl, C-heterocycloalkenyl, C-halo, C-CN, C-R4, CNY1Y2, COH, CZ2R, CC(O)R, CC(O)OR5, CC(O)NY1Y2, CN(R8)C(O)R, CN(R6)C(O)OR7, CN(R6)C(O)NY3Y4, CN(R6)SO2NY3Y4, CN(R6)SO2R, CSO2NY3Y4, C-NO2, or C-alkenyl or C-alkynyl optionally substituted by ≥1 aryl, cyano, halo, hydroxy, heteroaryl, heterocycloalkyl, nitro, -C(O)NY1Y2, -C(O)OR5, -NNY1Y2, -N(R6)C(O)R7, -N(R6)C(O)NY3Y4, -N(R6)C(O)OR7, -N(R6)SO2R7, -N(R6)SO2NY3Y4, -SO2NY1Y2 and -Z2R4. Y1 and Y2 = H, alkenyl, aryl, cycloalkyl, heteroaryl or alkyl optionally substituted by ≥1 aryl, halo, heteroaryl, heterocycloalkyl, hydroxy, -C(O)NY3Y4, -C(O)OR5, NY3Y4, -N(R6)C(O)R7, -N(R6)C(O)NY3Y4, -N(R6)SO2R7, -N(R6)SO2NY3Y4 and -OR7, or the group -NY1Y2

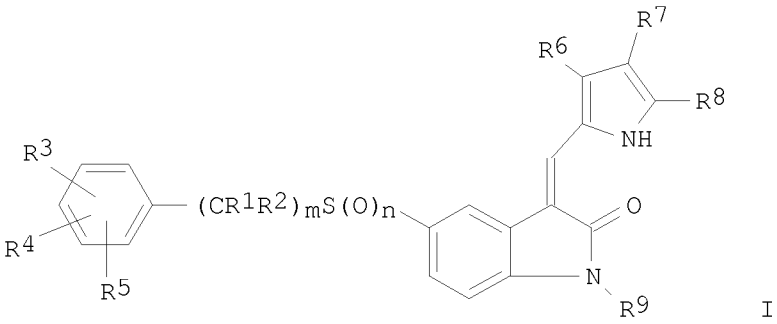
may form a cyclic amine. Y3 and Y4 = H, alkenyl, alkyl, aryl, arylalkyl, cycloalkyl, heteroaryl or heteroarylalkyl; or the group -NY3Y4 may form a cyclic amine; Z1 = O or S; Z2 = O or S(O)n; Z3 = O, S(O)n, NR6; n = 0-2.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:927188 CAPLUS
DN 138:14005
TI Preparation of 5-aralkylsulfonyl-3-(pyrrol-2-ylmethylidene)-2-indolinone derivatives as kinase inhibitors
IN Cui, Jingrong; Ramphal, Yudhi; Liang, Congxin; Sun, Li; Wei, Chung Chen; Tang, Peng Cho
PA USA
SO PCT Int. Appl., 479 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002096361	A2	20021205	WO 2002-US16841	20020530
	WO 2002096361	A3	20030313		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002303892	A1	20021209	AU 2002-303892	20020530
	US 20030125370	A1	20030703	US 2002-157007	20020530
	US 6599902	B2	20030729		
PRAI	US 2001-294544P	P	20010530		
	US 2001-328408P	P	20011010		
	WO 2002-US16841	W	20020530		

OS MARPAT 138:14005
GI



I

AB The present invention relates to certain 5-aralkylsulfonyl-3-(pyrrol-2-ylmethylidene)-2-indolinone derivs. (shown as I; see below for variable definitions; e.g. 2,4-dimethyl-5-(2-oxo-5-phenylmethanesulfonyl-1,2-dihydroindol-(3Z)-ylidenemethyl)-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide) that inhibit kinases (no data), in particular

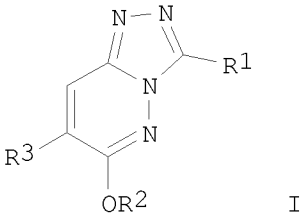
met kinase. Pharmaceutical compns. comprising these compds., methods of treating diseases mediated by kinases using pharmaceutical compns. comprising these compds., and methods of preparing them are also disclosed. In I: n = 0-2; m = 1-3; R1 and R2 = H or alkyl; R3, R4, and R5 = H, halo, alkyl, cycloalkyl, haloalkyl, hydroxy, alkoxy, alkoxycarbonyl, haloalkoxy, cyano, carboxy, carboxyalkyl, nitro, aryl, aryloxy, heteroaryl, heteroaryloxy, -(alkylene)-CONR10R11, -CONR10R11, or - NR10R11 (R10 is H or alkyl, and R11 is aryl, heteroaryl, heterocycle, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, acetylalkyl, cyanoalkyl, carboxyalkyl, alkoxycarbonylalkyl, heteroaralkyl, aralkyl, or heterocyclylalkyl wherein the alkyl chain in aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aralkyl, heteroaralkyl, or heterocyclylalkyl is optionally substituted with one or two hydroxy, or R10 and R11 together with the N atom to which they are attached combine to form saturated or unsatd. heterocycloamino). R6 is H, alkyl, cycloalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, carboxyalkyl, heterocyclylalkyl, aryl, heteroaryl, carboxy, alkoxycarbonyl, heterocyclylcarbonyl, aminoalkylcarbonyl, alkylaminoalkylcarbonyl, dialkylaminoalkylcarbonyl, -CONR10R11 or -(alkylene)-CONR10R11. R7 and R8 = H, alkyl, cycloalkyl, heterocyclylalkyl, -COR12, -(alkylene)-COR12 (R12 = alkoxy, hydroxy, or heterocycle, alkylamino, dialkylamino), -SO2R14, -CONR13R14, or -(alkylene)-CONR13R14 (R13 is H or alkyl, and R14 is aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, acetylalkyl, cyanoalkyl, carboxyalkyl, alkoxycarbonylalkyl, heteroaralkyl, or heterocyclylalkyl wherein the alkyl chain in aminoalkyl, heteroaralkyl, heteroaralkyl, or heterocyclylalkyl is optionally substituted with one or two hydroxy group(s), or when R13 and R14 are attached to a N atom R13 and R14 together with the N atom to which they are attached form saturated or unsatd. heterocycloamino). R6 and R7 or R7 and R8 can combine to form a saturated or unsatd. 5 to 8 membered ring; and R9 is: H or alkyl; -PO(OR15)2 where each R15 = H or alkyl; -COR16 where R16 is H or alkyl; or -CHR17NR18R19 where R17 is H or alkyl, and R18 and R19 = H or alkyl or R18 and R19 together with the N atom to which they are attached form heterocycloamino. Although the methods of preparation are not claimed, 375 example prepns. of I plus addnl. prepns. of intermediates are included.

L2 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:814133 CAPLUS
DN 137:337904
TI Preparation of triazolo[4,3-b]pyridazines as inhibitors of Akt, a serine/threonine protein kinase.
IN Carling, William Robert; Castro Pineiro, Jose Luis; Moore, Kevin William
PA Merck Sharp & Dohme Limited, UK
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083675	A2	20021024	WO 2002-GB1649	20020408
WO 2002083675	A3	20021205		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002251266 A1 20021028 AU 2002-251266 20020408
US 20040116432 A1 20040617 US 2003-473763 20031002
US 6960584 B2 20051101
PRAI US 2001-282806P P 20010410
WO 2002-GB1649 W 20020408
OS MARPAT 137:337904
GI



I

AB Title compds. [I; R1 = (substituted) Ph, furyl, thienyl, pyridinyl; R2 = (substituted) aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl; R3 = (substituted) cycloalkyl, aryl], were prepared Thus, 3,6-dichloro-4-phenylpyridazine (preparation given), benzoic hydrazide, and triethylammonium chloride were heated together at reflux in xylene for 3 days; More benzoic hydrazide was added and the mixture was heated as before for another day to give 36% 6-chloro-3,7-diphenyl-1,2,3-triazolo[4,3-b]pyridazine. This was added to a prestirred mixture of ethylene glycol and NaH in DMF followed by heating at 60° for 8 h and stirring at room temperature for 10 h to give 6-(2-hydroxyethyl)oxy-3,7-diphenyl-1,2,4-triazolo[4,3-b] pyridazine. This inhibited Akt-1 with IC50 = 15.9 μM.

L2 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:813872 CAPLUS
DN 137:333127
TI A method of treating cancer using a selective inhibitor of serine/threonine protein kinase Akt
IN Barnett, Stanley F.; Defeo-Jones, Deborah; Haskell, Kathleen M.; Huber, Hans E.; Nahas, Deborah D.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083064	A2	20021024	WO 2002-US10879	20020408
WO 2002083064	A3	20030227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2442264	A1	20021024	CA 2002-2442264	20020408

	AU 2002307163	A1	20021028	AU 2002-307163	20020408
	AU 2002307163	B2	20060629		
	EP 1379250	A2	20040114	EP 2002-762009	20020408
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004527531	T	20040909	JP 2002-580869	20020408
	US 20040106540	A1	20040603	US 2003-473791	20031002
PRAI	US 2001-282783P	P	20010410		
	WO 2002-US10879	W	20020408		

OS MARPAT 137:333127

AB The present invention is directed to a method of treating cancer which comprises administration of a compound which selectively inhibits the activity of one or two of the isoforms of Akt, a serine/threonine protein kinase. The invention is particularly directed to the method wherein the compound is dependent on the presence of the pleckstrin homol. domain (PH) of Akt for its inhibitory activity. Akt inhibitor N'-(7-Cyclobutyl-3-phenyl-1,2,4-triazolo[4,3-b]pyridazin-6-yl)-2,2,N,N-tetramethylpropane-1,3-diamine was prepared from 3,6-dichloropyridazine and tested against human Akt isoforms and ΔPH-Akt1.

L2 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:31440 CAPLUS

DN 136:102386

TI Preparation and use of 4-heteroaryl-3-heteroarylidenyl-2-indolinones and their use as protein kinase inhibitors

IN Tang, Peng Cho; Wei, Chung Chen; Huang, Ping; Cui, Jingron

PA Sugen, Inc., USA

SO PCT Int. Appl., 164 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002002551	A1	20020110	WO 2001-US20768	20010629
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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	CA 2414468	A1	20020110	CA 2001-2414468	20010629
	US 20020187978	A1	20021212	US 2001-894902	20010629
	US 6635640	B2	20031021		
	EP 1296975	A1	20030402	EP 2001-948830	20010629
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004502686	T	20040129	JP 2002-507803	20010629
	US 20040097497	A1	20040520	US 2003-648810	20030827
	US 7053086	B2	20060530		
PRAI	US 2000-215654P	P	20000630		
	US 2001-894902	A3	20010629		
	WO 2001-US20768	W	20010629		

OS MARPAT 136:102386

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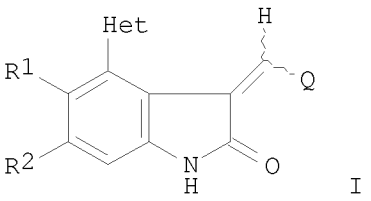

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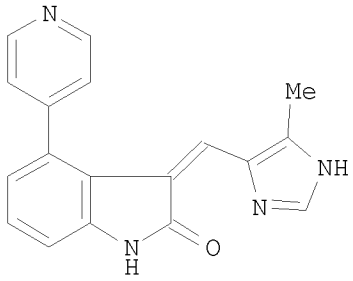


II

AB Title compds. I [R1-2 = H, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, etc.; Het = (un)substituted aromatic heterocycle containing at least one and not more than two N atoms, tetrahydro(thio)pyranyl, (thio)morpholino, piperidinyl, piperazinyl, tetrazolyl, etc.; Q = (un)substituted aromatic heterocycle containing not more than two N atoms, 5-membered ring (un)substituted heterocycle containing N, O or S, e.g., imidazolyl, pyrrolyl, indolyl, etc.] with some exceptions, were prepared Included are 75 synthetic examples and results for several protein tyrosine kinase assays for those compds. For instance, 4-bromoindole was coupled to bis(pinacolato)diborane (DMSO, KOAc, PdCl2(dppf)•CH2Cl2, 80°C, 22 h). The resulting dioxaborolane was coupled to 4-bromopyridine•HCl (THF, Pd(PPh3)4, NaOH, 70°C, 6 h) to give the indole which was treated with C5H5N•Br3 (t-BuOH/EtOH/H2O, 1h) followed by zinc (stirred 1 addnl. hour) to give 4-(pyridin-4-yl)-1,3-dyhydroindol-2-one as a yellow solid. Condensation of this intermediate with 5-methylimidazole-4-carboxaldehyde (EtOH, piperidine, 2 days) afforded II. II had IC50 = 4.88 mM for FGFR-1 tyrosine kinase and 0.03 mM for cdk2/cyclin A tyrosine kinase. I are useful in treating cancer, immunol. disorders, etc.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:489395 CAPLUS
DN 135:92651
TI Preparation of azaindoles as protein kinase inhibitors
IN Cox, Paul Joseph; Majid, Tahir Nadeem; Lai, Justine Yeun Quai; Morley, Andrew David; Amendola, Shelley; Deprets, Stephanie; Edlin, Chris
PA Aventis Pharma Ltd., UK
SO PCT Int. Appl., 270 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001047922	A2	20010705	WO 2000-GB4993	20001227
WO 2001047922	A3	20020117		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

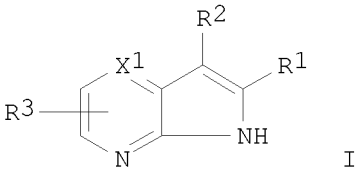
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2395593	A1	20010705	CA 2000-2395593	20001227
EP 1263759	A2	20021211	EP 2000-985695	20001227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2000017038	A	20030107	BR 2000-17038	20001227
HU 2002003895	A2	20030228	HU 2002-3895	20001227
HU 2002003895	A3	20040928		
EE 200200343	A	20030616	EE 2002-343	20001227
JP 2003519144	T	20030617	JP 2001-549392	20001227
NZ 519121	A	20040528	NZ 2000-519121	20001227
AU 777717	B2	20041028	AU 2001-22094	20001227
CN 1615873	A	20050518	CN 2004-10078969	20001227
ZA 2002004126	A	20030825	ZA 2002-4126	20020523
BG 106836	A	20030430	BG 2002-106836	20020618
NO 2002003032	A	20020621	NO 2002-3032	20020621
NO 323766	B1	20070702		
MX 2002PA06338	A	20021213	MX 2002-PA6338	20020621
KR 755622	B1	20070904	KR 2002-708150	20020622
US 20040009983	A1	20040115	US 2002-178667	20020624
US 6770643	B2	20040803		
US 20040198737	A1	20041007	US 2004-827978	20040420
US 7227020	B2	20070605		
NO 2006006017	A	20020621	NO 2006-6017	20061227
KR 2007050103	A	20070514	KR 2007-709139	20070423

PRAI GB 1999-30698 A 19991224
US 2000-215818P P 20000705
WO 2000-GB4993 W 20001227
KR 2002-708150 A3 20020622
US 2002-178667 A3 20020624

OS MARPAT 135:92651

GI



I

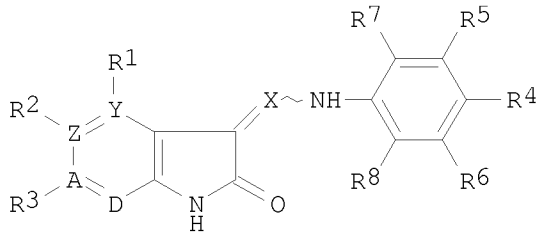
AB The invention is directed to compns. containing physiol. active compds. of general formula [I; wherein R1 is (un)substituted aryl or heteroaryl; R2 represents hydrogen, acyl, cyano, halo, lower alkenyl or lower alkyl optionally substituted by a substituent selected from cyano, heteroaryl, heterocycloalkyl, -Z1R8, -CONY3Y4,-CO2R8,-NY3Y4, -N(R6)COR7, -N(R6)CONY3Y4, -N(R6)CO2R7, -N(R6)SO2R7, -N(R6)SO2NY3Y4 and one or more halogen atoms; R3 represents hydrogen, aryl, cyano, halo, heteroaryl, lower alkyl, -CO2R5 or -CONY3Y4; and X1 represents N, CH, C-halo, C-CN, C-R7, C-NY3Y4, C-OH, C-Z2R7, C-CO2R5, C-CONY3Y4, C-N(R8)COR7, C-SO2NY3Y4, C-N(R8)SO2R7, C-alkenyl, C-alkynyl or C-NO2; wherein R5 represents hydrogen, alkyl, alkenyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl; R6 represents hydrogen or lower alkyl; R7 represents alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl or heterocycloalkylalkyl; R8 represents hydrogen or lower alkyl; represents; Y3 and Y4 are independently hydrogen, alkenyl, alkyl, aryl, arylalkyl, cycloalkyl, heteroaryl or heteroarylalkyl; or the group

-NY3Y4 may form a cyclic amine; Z1 represents O or S; Z2 represents O or S(O)n; n is zero or an integer 1 or 2] and their prodrugs, and pharmaceutically acceptable salts and solvates of such compds. and their prodrugs. These compds. have valuable pharmaceutical properties, in particular the ability to inhibit protein kinases, especially Syk kinase, and are useful for the treatment of asthma, psoriasis, joint inflammation, and inflammatory bowel disease. Thus, a stirred solution of diisopropylamine (59.9 mL) in THF (1,400 mL), at -15 °C and under nitrogen, was treated with a solution of n-butyllithium in hexanes (131 mL, 1.6 M) over 25 min at <-10°. After stirring for 30 min the mixture was treated with methylpyrazine (26.8 g) over 15 min, then stirred for 1 h and then treated with a solution of 5-methoxy-1-methyl-1H-indole-3-carbonitrile (53 g) in THF (600 mL) over 1 h at <-10°, and the reaction mixture was allowed to warm to room temperature over 2 h and then stood overnight to give, after workup and flash chromatog., 6-(5-Methoxy-1-methyl-1H-indol-3-yl)-5H-pyrrolo[2,3-b]pyrazine (19.4 g) as a gray solid. I showed IC50 of 10-100 nM against Syk kinase.

L2 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:688216 CAPLUS
DN 133:266726
TI Preparation of 3-(anilinomethylene)oxindoles and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors
IN Glennon, Kimberley Caroline; Kuyper, Lee Frederick; Lackey, Karen Elizabeth; McNutt, Robert Walton, Jr.
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000056710	A1	20000928	WO 2000-US5057	20000228
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1165514	A1	20020102	EP 2000-913643	20000228
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6350747	B1	20020226	US 2000-514528	20000228
	JP 2002540097	T	20021126	JP 2000-606572	20000228
	JP 3824866	B2	20060920		
	US 6498176	B1	20021224	US 2001-914063	20010822
	US 20020099071	A1	20020725	US 2001-966318	20010927
	US 6818632	B2	20041116		
	US 20040191210	A1	20040930	US 2003-742435	20031219
	US 7129253	B2	20061031		
PRAI	GB 1999-4933	A	19990304		
	US 2000-514528	A3	20000228		
	WO 2000-US5057	W	20000228		
	US 2001-966318	A3	20010927		

OS MARPAT 133:266726
GI



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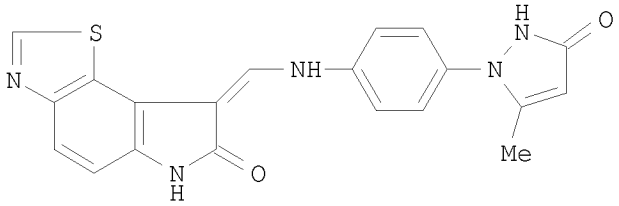

II

AB The title compds. (I) [wherein X = N, CH, CCF3, or C(aliphatic); Y, Z, A, and D = C or N, and the number of N ≤ 1; R1 = H, aliphatic, SH, hydroxy(aliphatic), aryl(aliphatic), cycloalkyl(aliphatic), heterocyclyl(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxycarbonyl, halo, CN, or NO2; R2 = H, aliphatic, hydroxyimino aliphatic, alkoxy(carbonyl), hydroxyaliph., aryl(oxycarbonyl), heterocyclyl, (un)substituted CONH2, NH2, or SO2NH2, halo, OH, NO2, aliphatic sulfonyl, etc.; or R1 and R2 are joined to form an (un)substituted fused heterocyclic ring; R3 = H, aliphatic, hydroxy(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxy, aryl(oxy), hydroxyaryl, (hydroxy)heterocyclyl, heterocyclyloxy, or halo; or R2 and R3 are joined to form an (un)substituted fused heterocyclic ring; R4 = SO3H, (aliphatic)sulfonyl(aliphatic), (un)substituted SO2NH2, NH2, CONH2, etc.; R5 = H; or R4 and R5 are joined to form an (un)substituted fused heterocyclic ring] were prepared via standard synthetic methods and solution phase library techniques as vascular endothelial growth factor receptor type 2 (VEGFR-2), cyclin dependent kinase 2 (CDK2), tyrosine kinase Tie-2 receptor, and colony-stimulating factor 1 receptor kinase (c-fms) inhibitors. For example, a mixture of 8-dimethylaminomethylene-6,8-dihydro-1-thia-3,6-diaza-as-indacene-7-one (preparation given) and 2-(4-aminophenyl)-3-methylpyrazolin-5-one in absolute EtOH was heated with stirring at 90°C for 16 h to give (Z)-II (83%). In substrate phosphorylation assays, II inhibited VEGFR-2 and CDK2 with IC50 values of 1-10 μM and 11-50 μM, resp. I are useful as therapeutic agents in disease states alleviated by the inhibition or antagonism of protein kinase activated signalling pathways in general, and in particular in the pathol. processes which involve aberrant cellular proliferation, such as tumor growth, restenosis, atherosclerosis, and thrombosis. I are particularly useful for suppressing tumor growth by inhibiting tumor-related angiogenesis.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:666732 CAPLUS
DN 133:252418
TI Preparation of anilinomethylene aza-oxindoles and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors
IN Harris, Philip Anthony; Kuyper, Lee Frederick; Lackey, Karen Elizabeth;

Veal, James Marvin
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000055159	A2	20000921	WO 2000-US5583	20000303
WO 2000055159	A3	20011129		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1180105	A2	20020220	EP 2000-917713	20000303
EP 1180105	B1	20030514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003502280	T	20030121	JP 2000-605588	20000303
AT 240328	T	20030515	AT 2000-917713	20000303
ES 2199156	T3	20040216	ES 2000-917713	20000303
US 6624171	B1	20030923	US 2001-914393	20010828
US 20040072836	A1	20040415	US 2003-669400	20030923
US 6815439	B2	20041109		
PRAI GB 1999-4995	A	19990304		
WO 2000-US5583	W	20000303		
US 2001-914393	A1	20010828		

OS MARPAT 133:252418
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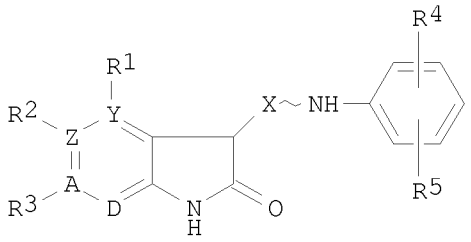

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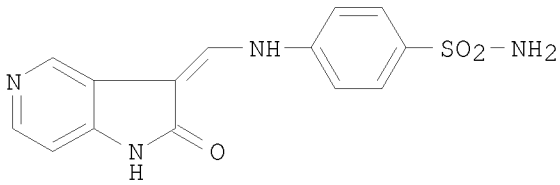

II

AB The title compds. (I) [wherein X = N, CH, CCF3, or C(aliphatic); Y, Z, A, and D = C or N, and the number of N ≤ 1; R1 = H, aliphatic, SH,

hydroxy(aliphatic), aryl(aliphatic), cycloalkyl(aliphatic), heterocyclyl(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxycarbonyl, halo, CN, or NO2; R2 = H, aliphatic, hydroxyimino aliphatic, alkoxy(carbonyl), hydroxyaliph., aryl(oxycarbonyl), heterocyclyl, (un)substituted CONH2, NH2, or SO2NH2, halo, OH, NO2, aliphatic sulfonyl, etc.; or R1 and R2 are joined to form an (un)substituted fused heterocyclic ring; R3 = H, aliphatic, hydroxy(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxy, aryl(oxy), hydroxyaryl, (hydroxy)heterocyclyl, heterocyclyloxy, or halo; or R2 and R3 are joined to form an (un)substituted fused heterocyclic ring; R4 = SO3H, (aliphatic)sulfonyl(aliphatic), (un)substituted SO2NH2, NH2, CONH2, etc.; R5 = H; or R4 and R5 are joined to form an (un)substituted fused heterocyclic ring] were prepared via standard synthetic methods and solution phase library techniques as cyclin dependent kinase 2 (CDK2), colony-stimulating factor 1 receptor kinase (c-fms), and vascular endothelial growth factor receptor type 2 (VEGFR-2) inhibitors. For example, 1,5-diazainden-2-one•HBr was reacted with N,N-dimethylformamide-di-t-Bu acetal in DMF to give the 3-dimethylaminomethylene derivative, which was treated with sulfanilamide in EtOH with HCl to form (Z)-II. In substrate phosphorylation assays, II inhibited CDK2 and VEGFR-2 with IC50 values of 0.01-0.1 μM and 1.0-10 μM, resp. I are useful as therapeutic agents in disease states alleviated by the inhibition or antagonism of protein kinase activated signalling pathways in general, and in particular in the pathol. processes which involve aberrant cellular proliferation, such as tumor growth, restenosis, atherosclerosis, and thrombosis. I are particularly useful for the prevention of chemotherapy-induced alopecia.

L2 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:303390 CAPLUS
DN 133:68373
TI Pharmacological properties of Y-27632, a specific inhibitor of Rho-associated kinases
AU Ishizaki, Toshimasa; Uehata, Masayoshi; Tamechika, Ichiro; Keel, Jeongsin; Nonomura, Kimiko; Maekawa, Midori; Narumiya, Shuh
CS Department of Pharmacology, Faculty of Medicine, Kyoto University, Kyoto, Japan
SO Molecular Pharmacology (2000), 57(5), 976-983
CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Y-27632 [(+)-(R)-trans-4-(1-aminoethyl)-N-(4-pyridyl)cyclohexan ecarboxamide dihydrochloride] is widely used as a specific inhibitor of the Rho-associated coiled-coil forming protein serine/threonine kinase (ROCK) family of protein kinases. This study examined the inhibition mechanism and profile of actions of Y-27632 and a related compound, Y-30141 [(+)-(R)-trans-4-(1-aminoethyl)-N-(1H-pyrrolo[2,3-b] pyridin-4-yl)cyclohexanecarboxamide dihydrochloride]. Y-27632 and Y-30141 inhibited the kinase activity of both ROCK-I and ROCK-II in vitro, and this inhibition was reversed by ATP in a competitive manner. This suggests that these compds. inhibit the kinases by binding to the catalytic site. Their affinities for ROCK kinases as determined by Ki values were at least 20 to 30 times higher than those for two other Rho effector kinases, citron kinase and protein kinase PKN. [3H]Y-30141 was taken up by cells in a temperature- and time-dependent and saturable manner, and this uptake was competed with unlabeled Y-27632. No concentrated accumulation was found, suggesting that the uptake is a carrier-mediated facilitated diffusion. Y-27632 abolished stress fibers in Swiss 3T3 cells at 10

μM, but the G1-S phase transition of the cell cycle and cytokinesis were little affected at this concentration Y-30141 was 10 times more potent than Y-27632 in inhibiting the kinase activity and stress fiber formation, and it caused significant delay in the G1-S transition and inhibition of cytokinesis at 10 μM.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT